LETTERS TO THE EDITOR

Coagulation abnormalities after Fontan procedures

To the Editor:

We read with interest the article by Jahangiri and associates in the June 1997 issue of the Journal (1997;113: 989-93). The concept of coagulation factor abnormalities in children after Fontan procedures is not new and was originally described by Cromme-Dijkhuis and associates[1, 2] in 1990 and 1993. In two cross-sectional surveys of children after Fontan procedures, Cromme-Dijkhuis and colleagues described multiple coagulation factor abnormalities involving both procoagulant and anticoagulant proteins. The authors noted that these abnormalities tended to resolve as duration of follow-up lengthened. However, closer examination of the Cromme-Dijkhuis articles revealed that the reference ranges used by the authors were not age-appropriate.[3] The majority of the plasma coagulation factor concentrations in these children were in fact normal for age. The apparent normalization with time reflected that with increasing age the children "grew into" the adult reference ranges that had been inappropriately applied previously. However, six of 19 patients in the Cromme-Dijkhuis series had higher thrombin-antithrombin (TAT) complexes than the age-appropriate normal ranges. Increased TAT complexes suggests a prothrombotic condition, although the mechanism in this instance remains unknown.

Unfortunately, Jahangiri and associates seem to have made the same error as Cromme-Dijkhuis and colleagues. In the Jahangiri article, the authors do not describe the source of their reference ranges. The normal ranges quoted are adult reference ranges and are not applicable to the patient population in question. The lower limit of normal for children 1 to 5 years of age is as low as 0.4 U/ml, in contrast to the 0.63 U/ml used by the authors.[3] It is likely that multiple age-related normal ranges need to be applied to the study population. The actual serum concentrations of the patients are not stated, and it is likely that many of the children believed to have abnormal values may be within the appropriate normal ranges. This would drastically alter the results and conclusions of this article.

There are many pitfalls to suggesting that patients have coagulation abnormalities. Testing in the presence of active thrombus may give false positive results. The methods used in collecting, processing, and assaying samples all need rigorous control. The use of accurate normative data is crucial to the definition of *abnormal.* The concept of developmental hemostasis is well established, and published normal ranges exist for premature and term infants, as well as children of all ages.[3-5]

Whether children who have had the Fontan procedure have a true prothrombotic condition, either congenital or acquired, is uncertain. Prospective cohort studies performed with appropriate techniques and compared with age-appropriate normative data will answer the question. The current study by Jahangiri and colleagues, because of major methodologic flaws, does not.

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Reply to the Editor:

We are aware of the excellent work of Dr. Andrew in the field of coagulation in childhood. The normal ranges quoted in the article were provided by the Thrombosis Research Institute at the Royal Brompton Hospital. Drs. Monagle and Andrew have quoted a normal range for children between 1 and 5 years of age. In our study the median age at the time of the Fontan repair was 6.2 years and the median time from the Fontan repair to the time of the study was 4.9 years. The normal range for children 1 to 5 years old, therefore, is not applicable to all the patients in this group. Considering the normal range for 6- to 10-year-old and 11- to 16-year-old patients published by Andrew and associates,[1] the published results hold (Table I). We have not noted any recovery of these coagulation factors.

None of the patients in the study had a history of thromboembolic episodes, and testing was not performed in the presence of active thrombus. This eliminates the chance for false positive results.

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